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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,991	11/03/2003	E. Itzhak Lerner	1662/61902	5352

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,991	LERNER ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *19-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/4/04;4/30/04;8/1806*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election with traverse of Group III, claims 1-3, drawn to a method of treating muscle spasms comprising administering an effective anti-spasmodic amount of tizanidine by a route of administration selected from the group consisting of buccal administration and sublingual administration is acknowledged. The restriction requirement made on the last Office Action between Group II and III is withdrawn in view of Applicants' amendment. Accordingly, claims 4-18 are being examined with elected Group III. However, the restriction between Group I drawn to a product claims and III&II (currently included in Group III) remains in effect because the product as claimed can be used in a materially different process because the product can be used to reduce somnolence in patients. Applicants argue that there is not a "serious burden" to examine all groups that are classified in the same class and subclass. This is not persuasive because restriction for examination purposes as indicated is proper because all these inventions listed in previous restriction requirement are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(b) the inventions require a different field of search (for example, electronic resources, or employing different search queries, non-patent literature search);

(c) the prior art applicable to one invention would not likely be applicable to another invention;

(d) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Accordingly, claims 1-18 are being examined on the merits and claims 19-31 are withdrawn from consideration because they are non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eichenberger et al. (U.S.Patent No. 4,053,617) in view of Patel et al. (U.S.Patent No. 6,569,463B1).

Eichenberger et al. teach that pharmaceutical compositions comprising 5-chloro-4-(2-imidazolin-2-yl-amino)-2,1,3-benaothiadiazole hydrochloride also known as ZANAFLEX® or tizanidine hydrochloride, useful for treating spastic conditions of muscles. Eichenberger et al. teaches the composition has a significant muscle relaxing effects. (abstract, column 1, claims 1 and 9). Eichenberger et al. illustrate oral formulations comprising tizanidine hydrochloride with excipients such as lactose colloidal silicon dioxide, microcrystalline cellulose and magnesium stearate. (Examples 1 and 2). Eichenberger et al. teach that the composition are preferred to administered in solid preparations such as tablet and capsules. (column 3, lines 10-13).

Eichenberger et al. do not expressly teach buccal or sublingual administration, percentages of the drug release and percentages of increased bioavailability of the drug, the populations of patients to be treated with observation of health care personnel

or medical records, the measuring techniques of the bioavailability of the drug, a single health care facility and therapy from a single doctor.

Patel et al. teach solid buccal or sublingual composition comprising tizanidine in a rapidly dissolvable and more solubilized state with improved absorption and/or bioavailability of tizanidine. (column 2, lines 15-40, claims 5-9,23,25, 34,35,37, 49 and 51). Patel et al. also teach that tizanidine composition comprising excipients such as lactose, microcrystalline cellulose, silica (silicone dioxide), stearic acid can be administered by buccal/sublingual route. (column 28, lines 31, 35, column 31, lines 1-10).

It would have been obvious to one of ordinary skill in the art to modify the teaching of Eichenberger et al. and employ ZANAFLEX® taught by Eichenberger et al. via buccal/sublingual administration for the treatment of muscle spasms because Patel et al. teach that solid oral tizanidine composition comprising excipients such as lactose, microcrystalline cellulose, silica (silicone dioxide) and stearic acid such as ZANAFEX® can be administered via buccal/sublingual route. Further, Patel et al. teach that the buccal or sublingual administration of a composition comprising tizanidine such as ZANAFLEX® improves the absorption and/or bioavailability of tizanidine. One would have been motivated to make such modification in order to achieve improved absorption and/or bioavailability of tizanidine by rapidly dissolving buccal or sublingual route of administration. There is a reasonable expectation of successfully treating muscle spasm with tizanidine formulation such as ZANAFLEX® via buccal/sublingual administration because Patel et al. teach that buccal/sublingual administration of

tizanidine formulation such as ZANAFLEX® increases bioavailability and improves absorption of tizanidine. The percentages of the drug release and increasing bioavailability of the drug is obvious result upon the administration of same active agent ZANAFLEX® via buccal/sublingual route taught by Patel et al. with increased bioavailability and absorption of tizanidine. Further, the populations of patients to be treated who have been administered tizanidine orally but do not respond well and are subsequently administered tizanidine sublingually or buccal is obvious because buccal/sublingual administration of tizanidine composition such as ZANAFLEX® increases bioavailability of tizanidine as taught by Patel et al. It would have been obvious to one of ordinary skill in the art at the time the invention was made to recommend buccal/sublingual administration rather than ingesting ZANAFLEX® to a patient having sub-therapeutic effect in order to achieve an expected benefit of improved absorption of tizanidine as taught by Patel et al. The patient population receiving the therapy at a single health care facility and the treatment receiving from a single doctor are all deemed oblivious because it is desirable in medical health system to have a patient receive a medical care from a single doctor particularly for a single disease symptom such as muscle spasm in order to decrease risks of duplicate and unnecessary treatment due to miss communication between doctors. Moreover, to have the patient attend a single medical facility is obvious because of various reasons, for example, development of a personal relationship between patient and the medical staff in a same location and it is convenient for the patient to report to the same location. Further, it provides central location of a medical profile that can be obtain/access easily

by medical staff or by the patient. The measuring technique of the bioavailability of the tizanidine is obvious because it is well within the skilled in the art and routine procedure. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Kim
Patent Examiner
Art Unit 1617

Jmk
June 24, 2007